The role of inhibition in hippocampal place cells

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The fundamental computation a single neuron performs is to integrate incoming excitatory and inhibitory inputs to decide whether to fire an action potential and feedback its activity into the network. Investigation of this synaptic computation requires access to the neuron subthreshold dynamics, whose state-of-art methodologies have remained unaltered for decades and are unrealistic for cell assemblies and behaving animals.

Instead of intracellular recording, we propose a method to optogenetically probe the membrane polarization of the cells with short depolarizing pulses using chronically implanted µLED probes (4 shanks with 3 µLED/shank). Light-sensitive neurons responded to one or more µLEDs and the spike numbers were used as a proxy for estimating relative changes of the membrane potential dynamics. Strikingly, induced spike responses gain sharply increased several-folds inside the preferred position (place fields) of the responsive cells. These results are compatible with a tuning curve model in the CA1 pyramidal cells where excitation and the inhibition display a concerted and reciprocal relationship. When optogenetic stimulation was probed on non-place cells, majority of the putative non-place cells showed place-related activity. Finally, we optically probed neurons around sharp wave-ripples (SPW-Rs), hippocampal events considered a key mechanism for memory consolidation and action planning. In the short time window of SPW-R, excitatory and inhibitory neurons increased in parallel. As expected, optogenetic probing of the CA1 networks showed that, in contrast to the large gain within place fields, responsivity of pyramidal cells showed a robust decrease during SPW-Rs.

We have developed a method for studying subthreshold dynamics of individual cells in chronic recordings using novel high-resolution optical stimulation as a proxy for the membrane polarization. These experiments disclosed a reciprocal interaction between inhibition and excitation along the place fields of CA1 and demonstrated that the same exact perturbation can bring about opposite responses during exploration and transient SPW-Rs.